

Is Physical Exercise a Core Therapeutical Element for Most Patients With Type 2 Diabetes?

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Over the last decade, growing scientific evidence has demonstrated that exercise is an effective therapeutic strategy for type 2 diabetes (1–12). According to position statements published by the American Diabetes Association, American College of Sports Medicine, and American Heart Association, exercise therapy should be part of a structured lifestyle intervention and include both aerobic and resistance training (13,14).

Physical activity is defined as any bodily movement produced by skeletal muscles that results in energy expenditure beyond resting expenditure. Exercise is a subset of physical activity that is planned, structured, repetitive, and purposeful in the sense that improvement or maintenance of physical fitness is the objective. As with pharmacological therapy, for aerobic or resistance exercise therapy it is necessary to prescribe the right dose (intensity, volume, and frequency) and to carefully consider the potential side effects and contraindications. The aim of this review is to discuss a correct approach to exercise therapy and to underline the beneficial effects, precautions, and limitations of the use of exercise in type 2 diabetic subjects. Another crucial point that merits discussion is the profound gap between the exercise therapy suggested by scientific guidelines and the applicability of it in the management of type 2 diabetes. Full

compliance with an exercise regimen requires high motivation and capability, both in the diabetes team operators/facilitators and in their patients, and is based on a strong therapeutic alliance. There are several obstacles in this virtuous process: lack of time and lack of confidence in the behavioral and motivation strategies of physicians and other diabetic team operators, unhealthy lifestyles of physicians who should advise exercise, and reluctance of sedentary diabetic patients to change their lifestyle, mainly due to poor self-efficacy or lack of time (15). The “no” side of this debate will discuss the evidence in the literature on the strategies that can reduce the gap and augment the clinical applicability of guidelines. In the “yes” side, we report the evidence that exercise works in the research setting and in the “no” side, that often exercise therapy fails in the primary care setting and what we should do to remedy the problem.

Discussion of the “yes” side of the debate

Several good motives, ranging from the pathophysiology of the disease to the demonstrated numerous beneficial effects for health and society, support the use of exercise as a core element in treatment of people with type 2 diabetes (1–14).

It is likely that most of the documented beneficial effects of exercise in type 2 diabetes are mediated by the increase of combined aerobic and resistance exercise

of muscle mass and strength (5,10,16), VO_{2max} (2,10,16), mitochondrial biogenesis (16), and insulin sensitivity (5,17,18). In subjects with type 2 diabetes, regular aerobic, resistance, or combined exercise training results in a decline in HbA_{1c} ranging from 0.51 to 0.73%, with a dose-dependent relationship (11). The amount of energy expenditure with exercise that produces the best dose/effect benefit ranges between 20 and 30 MET · h/week (3,10), corresponding to walking ~20–30 km/week at a speed of 4–5 km/h. However, beneficial effects can be obtained with a lesser effort, and for this reason the statements of scientific societies recommend at least 150 min/week moderate aerobic physical activity that should be combined with three weekly sessions of resistance exercise to increase muscle strength (13,14). The intensity of exercise should be in the moderate range (3–6 MET) because type 2 diabetic subjects are not familiar with high-intensity workouts and could easily drop out (15). Furthermore, moderate-intensity exercise can be sustained for a prolonged time, and training planned on moderate-intensity/long distances increases insulin sensitivity up to 14 days after the end of the last exercise session (18) and favors lipid consumption (19). However, training modalities for type 2 diabetic subjects are in constant evolution and necessitate further investigation. Very recently, continuous walking, performed at moderate intensity, has been compared with interval walking, structured in alternated 3-min repetitions at low and high intensity, in a small number of subjects with type 2 diabetes (20). Continuous walking in comparison with the control group improved glucose control, but interval walking was superior to energy expenditure–matched continuous walking for improving physical fitness, body composition, and glycemic control (20).

Regular exercise is generally recommended to maintain the beneficial effects of a weight loss (21,22), and levels of physical activity are often referred to as the best predictor of weight maintenance

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after significant weight loss (22,23). Interestingly, the 4-year results of the Look AHEAD (Action for Health in Diabetes) study demonstrate that the beneficial effects of the lifestyle intervention are independent of the degree of baseline obesity (12). Severely obese participants in the intensive lifestyle group had similar adherence, percentage of weight loss, and improvement in cardiovascular disease risk compared with less obese participants (12). Thus, behavioral weight loss programs, including exercise therapy, should be considered an effective option for this population (12). Recent data from the Look AHEAD study demonstrate also that in overweight adults, an intensive lifestyle intervention is associated with a greater likelihood of partial remission of type 2 diabetes compared with standard diabetes support and education (24).

The beneficial effects of exercise in type 2 diabetic subjects go well beyond improved glucose control and weight control; they also include the reduction of modifiable cardiovascular risk factors (10,12,13) and promote cardiorespiratory fitness (2,8,10,16). Several prospective studies have demonstrated a significant inverse relationship between cardiorespiratory fitness and all-cause risk of death in type 2 diabetic subjects (25,26). These studies show that an improvement of 1 MET ($3.5 \text{ mL} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ oxygen uptake) reduces the risk of death by ~18% in these subjects (25,26). Higher levels of physical activity have been associated with lower mortality risk in individuals with diabetes according to prospective studies (27). However, recently the Look AHEAD Study was stopped by the National Institutes of Health because the intensive lifestyle did not decrease occurrence of cardiovascular events, which was the primary study goal (28). At the time, participants had been in the intervention for up to 11 years and the intensive lifestyle intervention has been able to achieve and maintain weight loss by decreased caloric intake and increased physical activity (28). Thus, at present there is no conclusive evidence that regular exercise can significantly reduce cardiovascular events in overweight/obese type 2 diabetic subjects. Supervised exercise therapy is recommended also to subjects with previous cardiovascular events (14). However, screening for cardiovascular disease risk prior to starting exercise is important to minimize the risk of acute exercise-induced cardiovascular

complications. These aspects are discussed in detail in the joint position statement of the American Diabetes Association and the American College of Sports Medicine (14).

Regular exercise improves perceived health-related quality of life and mood status of type 2 diabetic subjects (29,30). These two beneficial effects support the World Health Organization concept that lifestyle interventions in obesity and type 2 diabetes have the potential to counteract the consequent social burden of depression (31). Patients with obesity or type 2 diabetes at the end of a multidisciplinary lifestyle intervention, in which exercise was a core element, report an improvement in their relationship with themselves and with others (32)—a distinctive result not achievable with pharmacological therapy. Strictly related to the quality of life is the circumstance that adults with type 2 diabetes often have limitations in mobility that increase with age. The recent results of the Look AHEAD study demonstrate that an intensive lifestyle intervention that produces weight loss and improves fitness could slow the loss of mobility in such patients (33).

The physician-patient relationship improves when exercise is used as a core strategy to treat type 2 diabetes because the counseling strategy to advise exercise entails empathy and listening (15,34). Directive models of diabetes care often result in noncompliance and failure to produce the desired behavior and outcomes (35). Exercise therapy, used as a core element of a multidisciplinary lifestyle intervention, considers patients as active participants in their own treatment and is a typical empowerment-based approach (36); as such, it is more appropriate for the management of chronic illnesses such as diabetes (37). To augment adhesion, exercise therapy should be individualized, considering patient preferences, and the strategy of the lifestyle motivators should be to change the patient's perception of exercise from a sacrifice to a pleasant experience (32,34).

Given the epidemic diffusion of type 2 diabetes, more research is necessary to analyze the cost-effectiveness of exercise interventions and the optimal modalities to deliver such interventions. At present, there is promising evidence that exercise therapy can reduce the costs of the National Health Service in preventing (38) and treating type 2 diabetes (3,39).

A post hoc subgroup cost analysis has estimated that the ideal financial savings are achieved when type 2 diabetic patients reach a leisure-time energy expenditure with exercise (mainly brisk walking) of 27 MET · h/week (3). It is critical to produce studies comparing the cost/utility of multidisciplinary lifestyle interventions with standard ambulatory diabetes care in clinical practice.

In conclusion, exercise can be considered a core element of type 2 diabetes therapy, characterized by several positive outcomes not entirely achievable by drug administration. However, it is challenging to convince sedentary obese individuals to change their lifestyle and to introduce exercise into a daily routine. In this regard, we need more studies reporting patients' views on barriers and facilitators to lifestyle change (32,40), identifying the psychological profile of those who are more resistant to the change (41) and the factors associated with success of lifestyle interventions (12,23). The current literature indicates that participants in lifestyle intervention appreciated the monitoring, encouragement, and accountability provided by the staff (32,40), that motivation is increased by a multidisciplinary approach including different professionals (physicians, nurses, dietitians, exercise physiologists, and educators) (40), that walking emerged as the most frequent form of physical activity (41), and that baseline depressive mood or low levels of health-related quality of life predict low attendance at exercise sessions (41), whereas greater self-reported physical activity (23) or attendance at exercise sessions (41) was the strongest correlate of weight loss. The "no" side of this debate will further discuss these aspects on the use of exercise in the clinical setting.

Discussion of the "no" side of the debate

There is no doubt that physical activity is important for diabetes therapy, and we have very good scientific evidence that an increase in physical activity helps to improve the outcome for diabetes patients (1–14,24), as it is also an important strategy for diabetes prevention (38,42). On the other hand, there is no doubt that implementing this strategy in clinical practice not always leads to the expected outcomes (28,43) so that, unfortunately, physical activity strategies in praxis reach only those who are already physically

active and there is no added value for the patients we have to reach: those who are physically inactive (42). Resistance training is confronted with a particularly high load of barriers, since the patient needs to have intensive training and supervision, attend a gym, and have a training plan. From this point of view, we could argue that “sports” in diabetes therapy fails to a large extent and that we need “improved” strategies to successfully increase physical activity (44).

Some of the strongest arguments for the “no” side have been presented in the introduction: “Full compliance with an exercise regimen requires high motivation and capability, both in the diabetic team operators/facilitators and in their patients, and is based on a strong therapeutic alliance.” There are additional indications of the barriers to exercise therapy. We have to build a very strong therapeutic bond and establish supervision for our patients, which is unrealistic in a medical environment where a physician sometimes has only 4 min counseling per patients and only 27 s to make a therapeutic decision (45). Furthermore, that “exercise therapy, used as a core element of a multidisciplinary lifestyle intervention, considers patients as active participants in their own treatment” also indicates why so many examples of exercise therapy in diabetic patients have failed. The physical activity intervention only works if patients become “active participants in their own treatment,” and this is only achievable with a structured behavioral support program. In conclusion, exercise therapy has often failed for the majority of diabetic patients in the primary care setting and only reaches a very tiny fraction of diabetic patients because it focuses too much on “exercise therapy” and lacks an adequate behavioral strategy as a pillar/support.

If we want to successfully increase physical activity in our patients, we can only succeed with behavioral intervention that has been adequately initiated. Exercise therapy has failed in the past because it has often been seen as a “therapy”—like taking a pill. As in most of our medication programs, it was missing adequate behavioral support and intervention strategy. Furthermore, exercise therapy, which focuses on resistance training, is the wrong way to reach the mass of our diabetic patients because the adherence to exercise among this patient group is low (1). Therefore, behavioral intervention

should be instituted and focus on an increase in physical activity, which is applicable to daily life and our environment and implementable in our home lifestyle. Why isn’t exercise therapy a core element for most patients with type 2 diabetes?

First, evolution has prepared us to “walk.” We are not “exercise” machines, but 10,000 years ago we had to walk probably >20,000/day for our daily survival. What is the situation today? We usually walk <5,000 steps/day (46), burn less energy, gain visceral adiposity, and accumulate chronic diseases like diabetes. Therefore, increasing the daily number of steps, supported by a group-based program, could be the most adequate intervention to increase physical activity and to improve glycemic control for all of our patients with diabetes and many other diseases (42,47,48). We can extrapolate that walking 10,000 steps/day from the age of 25 years may prevent many chronic diseases. Yates and coworkers have shown that a pragmatic structured education program that incorporates pedometer use is effective for improving glucose tolerance in subjects with impaired glucose tolerance (48). Interestingly, walking 1,000 steps more than your average per day—for a diabetic patient—reduces postprandial blood glucose by 1.6 mmol/L over a period of 2 years (48). This has the same effect on postprandial blood glucose as 1,000 mg metformin and can help to reduce the daily medication in diabetes treatment and associated therapies such as blood pressure medication or lipid-lowering drugs (49).

Second, behavior change must start at home. Behavior change affects our private life and relationships. Exercise therapy takes place in the wrong setting because you have to attend a gym as if you are going to a physician—often things you would like to avoid. On the other hand, walking steps is something that we do every day and in all situations of our life; it is already part of our daily lifestyle. Behavioral support can help us analyze the motivation to change lifestyle and to set new goals for lifestyle change. Action plans, as part of a behavioral strategy, can help patients reach goals and find ways to stimulate success and reduce relapse (50). For modification of physical activity behavior, it is much more successful to focus on the strategies that already exist in daily life than to focus on “therapeutic” strategies that take place outside the private

environment. The prescription of group-based brisk walking represents an equally effective intervention to modulate glycaemic control and cardiovascular risk profile in type 2 diabetic patients compared with more individualized medical fitness programs (51). Focusing on a behavioral strategy, setting new goals for the “daily step count” has a much higher chance of success of implementation in our daily life. The implementation strategy works better when education programs are based on self-management-oriented group, which supports patients to negotiate their goals and self-monitor their eating and exercise behavior and in analyzing barriers to behavior change (52). The role of health care professionals is to provide “behavioral support” and encouragement to the patients rather than treat them with specific exercise programs (42,44).

The key factor for successful diabetes care is the need to support sustained changes in lifestyle behaviors. However, achieving the required changes reliably is challenging. Both clinical weight loss programs (53,54) and real-world diabetes prevention programs vary widely in their ability to deliver weight loss or changes in physical activity. Sustained behavior change seems to be the best predictor of reliably increased effectiveness of lifestyle interventions (55). By accepting this, we can design diabetes chronic care management programs that will deliver the expected benefits and optimize cost-effectiveness in scalable, real-world disease management programs. A recent meta-analysis systematically developed evidence-based recommendations on supporting lifestyle change in people with type 2 diabetes including those with disease risk. Applying these recommendations may help guide the selection of intervention components in a way that maximizes the likely effectiveness of diabetes prevention programs (56).

Conclusions

Exercise is well known to be a potential lifestyle intervention to treat and prevent type 2 diabetes, especially when incorporated into a multidisciplinary lifestyle intervention. The evidence has been firmly established by several clinical trials. The challenge we have is to address the implementation of the evidence into clinical and public health practice—and here the question about the key items for changing lifestyle becomes relevant. Support for

behavior change is the predominant issue. Physical activity is a good sign of behavior change, but maintaining physical activity requires sustained behavioral support. The more natural the behavioral strategy, the more success it will have in increasing physical activity. Walking is natural from an evolutionary point of view and may have the potential to reach the masses with the right behavioral support program and incentives. Exercise therapy is a therapy associated with a disease that can be highly successful but needs an individualized strategy, and this is only applicable for a fraction of our patients. For it to be true that “physical activity becomes a core therapeutic element for most patients with type 2 diabetes,” we have to improve our understanding of the behavioral and physiological as well as contextual mechanisms of the development of diabetes and the disease itself. To reach every patient, we need an individual proposal that can become part of daily life. Nothing is more natural than walking, and to walk our diabetes away is effectively achievable. Patients who start walking may also decide later to walk to the exercise therapy to gain even more individual benefit. Future directions for research in this field should include the comparisons by randomized controlled trials of incorporating increased physical activity into daily activity versus specific prescription of aerobic and resistance exercise.

The focus of the intervention should be on lifestyle change rather than a prescription for exercise per se. Thus, exercise support should be part of a structured lifestyle intervention and include both aerobic and resistance training. The strength of physical activity is that it addresses the mechanistic basis of type 2 diabetes. Physical activity is therefore a core element in diabetes therapy, but effective behavioral support strategies are necessary to support the achievement of physical activity goals. Only when backed by a behavioral support strategy can physical activity express its maximum potential and become a leading element for every patient with type 2 diabetes. Sometimes, the importance of structured behavioral support is treated as a justification for not embracing exercise rather than discussed as a barrier that could/should be overcome through incorporation of diabetes educators, exercise physiologists, and lay coaches into diabetes care. It has been shown that the full spectrum of psychological and clinical

benefits from multidisciplinary lifestyle intervention is obtained when obese adults with or without type 2 diabetes attend both the exercise and the educational sessions (41). The multidisciplinary support is needed regardless of whether the recommendation is to engage in a structured exercise program or increase walking. The success of the behavioral intervention is strongly related to the enthusiasm and the motivation of the physicians and of the other operators of the multidisciplinary diabetes team who should not be sedentary and provide an example to their patients. It has been recently proven that physicians with a normal BMI in comparison with their overweight/obese colleagues are more likely to provide lifestyle advice (57). The Latin philosopher Lucius Annaeus Seneca (5–65 BC) wrote in one of his letters to Lucilio, “People believe more from their eyes than from their ears.”

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